



A service of the National Library of Medicine
and the National Institutes of Health

My NCBI [?](#)
[\[Sign In\]](#) [\[Register\]](#)

[All Databases](#)
[PubMed](#)
[Nucleotide](#)
[Protein](#)
[Genome](#)
[Structure](#)
[OMIM](#)
[PMC](#)
[Journals](#)
[Books](#)

 Search [PubMed](#)

 for [anti-CCR5](#)
[Preview](#)
[Go](#)
[Clear](#)
☒ Limits

☐ Preview/Index

☒ History

☐ Clipboard

☐ Details

Limits: Publication Date to 1996/06/14

- Search History will be lost after eight hours of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.
- Click on query # to add to strategy

[About Entrez](#)
[Text Version](#)
[Entrez PubMed](#)
[Overview](#)
[Help | FAQ](#)
[Tutorial](#)
[New/Noteworthy](#)
[E-Utilities](#)
[PubMed Services](#)
[Journals Database](#)
[MeSH Database](#)
[Single Citation Matcher](#)
[Batch Citation Matcher](#)
[Clinical Queries](#)
[Special Queries](#)
[LinkOut](#)
[My NCBI](#)

Search

Most Recent Queries

Time Result

#6 Search anti-CCR5 Field: All Fields , Limits: Publication Date to 1996/06/14	09:08:54	<u>0</u>
#4 Search Wu L 1997 and CCR5	07:06:04	<u>6</u>
#3 Search Wu L 1997	07:05:57	<u>166</u>
#2 Search 2D7 and LeukoSite, Inc.	06:36:55	<u>2</u>

[Clear History](#)

Related Resources

[Order Documents](#)
[NLM Mobile](#)
[NLM Catalog](#)
[NLM Gateway](#)
[TOXNET](#)
[Consumer Health](#)
[Clinical Alerts](#)
[ClinicalTrials.gov](#)
[PubMed Central](#)
[Write to the Help Desk](#)
[NCBI](#) | [NLM](#) | [NIH](#)
[Department of Health & Human Services](#)
[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Nov 29 2005 11:19:28

WEST Search History

DATE: Friday, December 02, 2005

Hide?	Set Name	Query	Hit Count
	<i>DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L20	L19	27
	<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L19	L18 and CCR5	288
<input type="checkbox"/>	L18	2D7	544
<input type="checkbox"/>	L17	L16 and CCR5 or CCCKR5	16
<input type="checkbox"/>	L16	Trkola A.in.	6
<input type="checkbox"/>	L15	L14 and CCR5	2
<input type="checkbox"/>	L14	Moore J.in.	1105
<input type="checkbox"/>	L13	Moore J.in.	1105
<input type="checkbox"/>	L12	L11 and CCR5	2
<input type="checkbox"/>	L11	Litwin V.in.	10
	<i>DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L10	US-6908734-B2.did.	1
	<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L9	L7 and CCR5	4
<input type="checkbox"/>	L8	L7 and 2D7	0
<input type="checkbox"/>	L7	Dragic T.in.	5
<input type="checkbox"/>	L6	Allaway G .in.	0
<input type="checkbox"/>	L5	L2 and 2D7	26
	<i>DB=PGPB; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L4	L2 and 2D7	0
<input type="checkbox"/>	L3	L2	0
	<i>DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L2	L1	63
	<i>DB=PGPB,USPT,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L1	anti adj CCR5	409

END OF SEARCH HISTORY

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1648BQL

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 4 OCT 03 MATHDI removed from STN
NEWS 5 OCT 04 CA/CAPLUS-Canadian Intellectual Property Office (CIPO) added
to core patent offices
NEWS 6 OCT 13 New CAS Information Use Policies Effective October 17, 2005
NEWS 7 OCT 17 STN(R) AnaVist(TM), Version 1.01, allows the export/download
of CAPLUS documents for use in third-party analysis and
visualization tools
NEWS 8 OCT 27 Free KWIC format extended in full-text databases
NEWS 9 OCT 27 DIOGENES content streamlined
NEWS 10 OCT 27 EPFULL enhanced with additional content
NEWS 11 NOV 14 CA/CAPLUS - Expanded coverage of German academic research
NEWS 12 NOV 30 REGISTRY/ZREGISTRY on STN(R) enhanced with experimental
spectral property data

NEWS EXPRESS NOVEMBER 18 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005.
V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
<http://download.cas.org/express/v8.0-Discover/>

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer
agreement. Please note that this agreement limits use to scientific
research. Use for software development or design or implementation
of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 09:27:50 ON 02 DEC 2005

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 09:28:01 ON 02 DEC 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 2 Dec 2005 VOL 143 ISS 24
FILE LAST UPDATED: 1 Dec 2005 (20051201/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

```
=> "anti-CCR5"
      389022 "ANTI"
          9 "ANTIS"
      389029 "ANTI"
          ("ANTI" OR "ANTIS")
      3804 "CCR5"
L1      98 "ANTI-CCR5"
          ("ANTI" (W) "CCR5")
```

```
=> 2D7 (1) L1
      87 2D7
L2      11 2D7 (L) L1
```

```
=> D L2 IBIB ABS 1-11
```

L2 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1046453 CAPLUS

DOCUMENT NUMBER: 142:175004

TITLE: Soluble chemokine CCR5 receptor is present in human plasma

AUTHOR(S): Tsimanis, Alexander; Kalinkovich, Alexander; Bentwich, Zvi

CORPORATE SOURCE: R. Ben-Ari Institute of Clinical Immunology and AIDS Center, Kaplan Medical Center, Hebrew University Hadassah Medical School, Rehovot, Israel

SOURCE: Immunology Letters (2005), 96(1), 55-61
CODEN: IMLED6; ISSN: 0165-2478

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In view of the natural resistance to infection by HIV and occasional delayed clin. manifestation of the disease, as also the fact that the virus is able to enter only cells that express CD4 and a co-receptor, we initiated a search for a soluble co-receptor that might compete with its membrane counterpart. Using a sandwich ELISA system, a soluble human CCR5 receptor (sCCR5) was indeed detected in the circulation. Immunopptn. of sCCR5-pos. plasma samples from Israelis of Ethiopian and non-Ethiopian origin with mAb 2D7, a conformation-dependent anti-CCR5 antibody, revealed the presence of a .apprx.22 kDa protein. A panel of antibodies directed against the membrane receptor was used to characterize the structure of the soluble CCR5: mAb CTC8, recognizing the N-terminal sequence of the protein, 10YDIN13; "multidomain" mAbs FAB181B and FAB183B that are dependent upon the presence of Q93 and D95 in ECL1 and K171 and E172 in ECL2A, and mAb FAB182B, recognizing the stretch 184YSQYQF189, which spans the C-terminal part of the second extracellular loop. The presence of short soluble CCR5 in human plasma has not been previously described. Among HIV-neg. non-Ethiopian Israelis, 20.4% were sCCR5-pos., as against only 10.5% in HIV-positives. However, 7.1% of HIV-neg. Ethiopian Israelis were sCCR5 pos., as were 5.6% HIV-positives. Plasma concns. of MIP-1 β , the CCR5 agonist, were twice as high in sCCR5-positives (140.8 \pm 25.8 pg/mL) as in the sCCR5-negatives (77.6

± 11.0 pg/mL, P = 0.0157). A significant pos. correlation between plasma levels of sCCR5 and MIP-1β was found (Fig. 4, r = 0.8, P < 0.0001).

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:900264 CAPLUS

DOCUMENT NUMBER: 140:92158

TITLE: Establishment of an HIV cell-cell fusion assay by using two genetically modified HeLa cell lines and reporter gene

AUTHOR(S): Sakamoto, Tatsunori; Ushijima, Hiroshi; Okitsu, Shoko; Suzuki, Eiko; Sakai, Koji; Morikawa, Shigeru; Muller, Werner E. G.

CORPORATE SOURCE: Graduate School of Medicine, Department of Developmental Medical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan

SOURCE: Journal of Virological Methods (2003), 114(2), 159-166
CODEN: JVMEDH; ISSN: 0166-0934

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Infection of human cells with the human immunodeficiency virus type I (HIV-1) can be mimicked by a fusion process between cells expressing the HIV envelope protein (Env) and cells expressing both human CD4 together with the appropriate human chemokine receptors. In this study, a T-tropic HIV cell-cell fusion assay was established that utilized CD4, human CXCR4 and HIV NL4-3 gp160 as fusion components and a T7 polymerase-activated luciferase as a reporter system. The HeLa T4 cells used, expressed CD4 and CXCR4, and the applied HeLa KS386 cells expressed HIV NL4-3 gp160. By combining HeLa T4 cells with HeLa KS386 cells, an approx. about 100- to 300-fold increase in luciferase activity could be elicited relative to the control. The addition of anti-CD4 monoclonal antibody (Mab) (RPA-T4) or anti-CXCR4 Mab (12G5) in the assay significantly inhibited the fusion event; in contrast, an **anti-CCR5** Mab (2D7) had no effect, indicating that the fusion assay was CD4 and CXCR4 dependent. In this report, fusion events could be monitored by both the luciferase reporter system and syncytia formation. Fusion events were monitored and compared using these two approaches. The luciferase reporter system was found to be more sensitive than syncytia formation. Moreover, compared with previous HIV fusion models, such as using recombinant vaccinia viruses, this system has several advantages, including simplicity and sensitivity. Finally, the system provides a powerful tool to study fusion mechanisms mediated by T-tropic HIV gp160, as well as to screen for fusion-blocking antibodies and antiviral agents.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:645176 CAPLUS

DOCUMENT NUMBER: 135:343097

TITLE: Adaptation to Blockade of Human Immunodeficiency Virus Type 1 Entry Imposed by the **Anti-CCR5** Monoclonal Antibody 2D7

AUTHOR(S): Aarons, Emma J.; Beddows, Simon; Willingham, Tim; Wu, Lijun; Koup, Richard A.

CORPORATE SOURCE: Department of Medicine, Division of Infectious Disease, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA

SOURCE: Virology (2001), 287(2), 382-390
CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The second extracellular loop (ECL2) domain of CC-chemokine receptor 5 (CCR5) has been proposed as a specific target site for therapeutic agents aimed at blocking CCR5-dependent entry by human immunodeficiency virus type I (HIV-1). We have adapted two CCR5-using HIV-1 isolates, prototypic

JR-CSF, and a primary isolate, 11-121, to replicate in vitro in the presence of high concns. of a monoclonal antibody (Mab 2D7) specific for the CCR5 ECL2 domain. The 75% inhibitory concns. (IC75) for the two 2D7-adapted isolates were approx. 100-fold higher than those for corresponding control isolates passaged without the Mab. Adapted isolates did not acquire the ability to use CXCR4, CCR3, or CCR1. Env clones derived from Mab 2D7-adapted JR-CSF showed several gp120 mutations that were not found in any of the control JR-CSF clones. The in vitro observations suggest that CCR5-using HIV-1 strains might also be able to adapt in vivo to evade an ECL2-blocking therapeutic agent. (c) 2001 Academic Press.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:399156 CAPLUS

DOCUMENT NUMBER: 135:179630

TITLE: Human α 1-acid glycoprotein binds to CCR5 expressed on the plasma membrane of human primary macrophages

AUTHOR(S): Atemezem, Aurelie; Mbemba, Elisabeth; Vassy, Roger;

CORPORATE SOURCE: Slimani, Hocine; Saffar, Line; Gattegno, Liliane
Laboratoire de Biologie Cellulaire, JE 2138, Faculte de Medecine Leonard de Vinci, Universite Paris XIII, Bobigny, 93017, Fr.

SOURCE: Biochemical Journal (2001), 356(1), 121-128

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have reported previously that human α 1-acid glycoprotein (AGP) inhibits the infection of human monocyte-derived macrophages (MDM) by R5 HIV-1, and that a disulfide-bridged peptide mimicking the clade B HIV-1 gp120 consensus V3 domain (V3Cs) binds specifically to CCR5 (the major co-receptor of R5 HIV strains) on these cells. The present study demonstrates that AGP binds specifically to MDM at high- and low-affinity binding sites with Kd values of 16 nM and 4.9 μ M resp. The fact that heat denaturation of AGP only partly inhibited this binding (43%) suggests that protein-protein interactions are involved, as well as AGP glycans which are resistant to heat denaturation. Mannan, but not dextran, is a significant inhibitor (52%) of this binding, and sequential exoglycosidase treatment of AGP, which exposes penultimate mannose residues, has a strong stimulatory effect (.apprx. 2.8-fold). Therefore AGP glycans (probably mannose residues) are involved, at least partly, in the binding of AGP to MDM. In addition, AGP inhibits the binding of V3Cs and macrophage inflammatory protein-1 β (MIP-1 β) to MDM. The **anti-CCR5** monoclonal antibody **2D7**, specific for the second extracellular loop of CCR5, also inhibited AGP binding (67%), whereas **anti-CCR5** antibodies specific for the C-terminus of CCR5 region had no effect. Native AGP, like V3Cs (but not heat-denatured AGP), binds to 46 and 33-36 kDa electroblotted AGP-bound MDM membrane ligands, characterized as CCR5 by their interactions with **anti-CCR5** antibodies and with MIP-1 β . Therefore both AGP glycans and MDM CCR5 are involved in the binding of AGP to MDM. This suggests that the inhibitory effect of AGP on the infection of human primary macrophages by R5 HIV-1 may be related to specific binding of AGP to a macrophage membrane lectin or lectin-like component and to CCR5.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:185460 CAPLUS

DOCUMENT NUMBER: 132:333214

TITLE: Inhibition of M-tropic HIV-1 infection by the fd phage-gene 3 protein with MIP-1 α -binding activity

AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa

CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering,

SOURCE: Kagoshima University, Kagoshima, 890-0063, Japan
Molecular Immunology (2000), Volume Date 1999, 36(18),
1249-1254
CODEN: MOIMD5; ISSN: 0161-5890
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CCR5 is a chemokine receptor with seven transmembrane-domains. It is expressed on T cells and macrophages and functions as the principal co-receptor for macrophage (M)-tropic strains of HIV-1. The **anti-CCR5** monoclonal antibody (mAb) **2D7** inhibits the binding and chemotaxis of the three natural β -chemokine ligands of CCR5, macrophage inflammatory protein (MIP)-1 α , MIP-1 β , and RANTES, to CCR5+ cells. The mAb also efficiently blocks the infectivity of several M-tropic and dual-tropic HIV-1 strains in vitro. In this study, the authors attempted to determine the peptide motif recognized with the **2D7** mAb. The authors isolated phage clones by panning a phage display library using **2D7** and identified three peptide motifs. One of these phage clones (M23) showed a marked inhibitory activity on HIV-1 infection. The unique sequence of 15 amino acids with an internal disulfide bond was inserted in the g3p of the M23 phage clone (M23-g3p). The M23-g3p was purified by fast-performance liquid chromatog. (FPLC). The authors show here that (1) M23-g3p was specifically recognized with **anti-CCR5** mAb; (2) M23-g3p showed inhibitory activity on the infectivity of M-tropic but not T-tropic HIV-1 strains; (3) M23-g3p bound to MIP-1 α , MIP-1 β , and RANTES but not MCP-1. These results suggested that the M23-g3p might mimic the CCR5-binding domain shared by β -chemokines, MIP-1 α , MIP-1 β , and RANTES as well as the HIV-1 infection.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:727861 CAPLUS
DOCUMENT NUMBER: 132:77404
TITLE: Relationship between Productive HIV-1 Infection of Macrophages and CCR5 Utilization
AUTHOR(S): Hung, Chia-Suei; Pontow, Suzanne; Ratner, Lee
CORPORATE SOURCE: Departments of Medicine, Pathology, Molecular Microbiology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Virology (1999), 264(2), 278-288
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HIV-1 isolates exhibit specificity for infection of immortalized T-cell lines and macrophages. The distinct cellular tropisms have been attributed to expression of coreceptors CXCR4 or CCR5, resp. However, it is unclear whether or not other tissue-specific determinants regulate entry. The current study uses a panel of viruses to analyze the relationship between CCR5 utilization and macrophage infection. Only chimeric viruses with the entire V3 loop from macrophage-tropic isolates, ADA or SF162, were able to infect macrophages. In contrast, chimeric viruses with smaller portions of the ADA V3 loop or the V3 loop of SF2, sufficient to allow CCR5 use, were insufficient for macrophage infection. PCR anal. showed that the defect in macrophage infection of the latter viruses was due to a defect in entry. Moreover, strains capable of infecting macrophages showed relative resistance to neutralization by **anti-CCR5** antibody, **2D7**, compared to strains which utilize CCR5 but are incapable of macrophage infection. (c) 1999 Academic Press.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:651420 CAPLUS
DOCUMENT NUMBER: 131:335588
TITLE: Enhanced expression, native purification, and

characterization of CCR5, a principal HIV-1 coreceptor
 AUTHOR(S): Mirzabekov, Tajib; Bannert, Norbert; Farzan, Michael;
 Hofmann, Wolfgang; Kolchinsky, Peter; Wu, Lijun;
 Wyatt, Richard; Sodroski, Joseph
 CORPORATE SOURCE: Department of Cancer Immunology and AIDS, Dana-Farber
 Cancer Institute, the Department of Pathology, Harvard
 Medical School, Harvard School of Public Health,
 Boston, MA, 02115, USA
 SOURCE: Journal of Biological Chemistry (1999), 274(40),
 28745-28750
 CODEN: JBCHA3; ISSN: 0021-9258
 PUBLISHER: American Society for Biochemistry and Molecular
 Biology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Seven-transmembrane segment, G protein-coupled receptors (GPCRs) play
 important roles in many biol. processes in which pharmaceutical
 intervention may be useful. High level expression and native purification of
 GPCRs are important steps in the biochem. and structural characterization
 of these mols. Here, we describe enhanced mammalian cell expression and
 purification of a codon-optimized variant of the chemokine receptor CCR5, a
 GPCR that plays a central role in the entry of the human immunodeficiency
 virus-1 (HIV-1) into immune cells. CCR5 could be solubilized in its
 native state as determined by its ability to be precipitated by **2D7**, a
 conformation-dependent **anti-CCR5** antibody, and by the
 HIV-1 gp 120 envelope glycoprotein. The **2D7** antibody recognized
 immature and mature forms of CCR5 equally, whereas gp 120 preferentially
 recognized the mature form, a result that underscores a role for
 posttranslational modification of CCR5 in its HIV-1 coreceptor function.
 The methods described herein contribute to the anal. of CCR5 and are
 likely to be applicable to many other GPCRs.
 REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1999:353334 CAPLUS
 DOCUMENT NUMBER: 131:169077
 TITLE: Peptide-motif analysis of phage clones selected by
anti-CCR5 monoclonal antibody (
2D7)
 AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki,
 Rieko; Nakashima, Hideki; Sugimura, Kazuhisa
 CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering,
 Kagoshima University, Kagoshima, 890-0065, Japan
 SOURCE: Peptide Science (1999), Volume Date 1998, 35th,
 489-492
 CODEN: PSCIFQ; ISSN: 1344-7661
 PUBLISHER: Protein Research Foundation
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The CCR5 is a chemokine receptor expressed on T cells and macrophages, and
 functions as the principal coreceptor for macrophage (M)-tropic HIV-1
 strains. An **anti-CCR5** monoclonal antibody termed
2D7 completely blocks the binding and chemotaxis of the three
 natural chemokine ligands of CCR5, MIP-1 α , MIP-1 β and RANTES to
 CCR5+ cells. The **2D7** also efficiency blocks the infectivity of
 several M-tropic and dual-tropic HIV-1 strains in vitro. In this study,
 we attempted to determine the peptide motif recognized by **2D7**. By
 panning a phage display library by **2D7**, we isolated phage clones
 which were specifically recognized by **2D7** and characterized
 these motifs.
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1999:263464 CAPLUS
 DOCUMENT NUMBER: 131:57557
 TITLE: Differential inhibition of human immunodeficiency
 virus type 1 fusion, gp120 binding, and CC-chemokine

activity by monoclonal antibodies to CCR5
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima,
Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.;
Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah
A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.;
Maddon, Paul J.; Dragic, Tatjana
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller
University, New York, NY, 10016, USA
SOURCE: Journal of Virology (1999), 73(5), 4145-4155
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (HIV-1) strains. The authors have isolated 6 new **anti-CCR5** murine monoclonal antibodies (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) HIV-1 entry, (2) HIV-1 envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit HIV-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited HIV-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and **2D7**, the most potent inhibitors of HIV-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting HIV-1 entry and fusion, PA12 but not PA14 was potentially synergistic when used in combination with **2D7**, RANTES, and CD4-IgG2, which inhibits HIV-1 attachment. The data support a model wherein HIV-1 entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These antibodies will be useful for further dissecting these events.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:810699 CAPLUS
DOCUMENT NUMBER: 130:167066
TITLE: Microglia express CCR5, CXCR4, and CCR3, but of these, CCR5 is the principal coreceptor for human immunodeficiency virus type 1 dementia isolates
AUTHOR(S): Albright, Andrew V.; Shieh, Joseph T. C.; Itoh, Takayuki; Lee, Benhur; Pleasure, David; O'Connor, Michael J.; Doms, Robert W.; Gonzalez-Scarano, Francisco
CORPORATE SOURCE: Departments of Neurology and Microbiology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-6146, USA
SOURCE: Journal of Virology (1999), 73(1), 205-213
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Microglia are the main human immunodeficiency virus (HIV) reservoir in the central nervous system and most likely play a major role in the development of HIV dementia (HIVD). To characterize human adult microglial chemokine receptors, the authors analyzed the expression and calcium signaling of CCR5, CCR3, and CXCR4 and their roles in HIV entry. Microglia expressed higher levels of CCR5 than of either CCR3 or CXCR4. Of these 3 chemokine receptors, only CCR5 and CXCR4 were able to transduce a signal in microglia in response to their resp. ligands, MIP-1 β and SDF-1 α , as recorded by single-cell calcium flux expts. The authors also found that CCR5 is the predominant coreceptor used for infection of

human adult microglia by the HIV type 1 dementia isolates HIV-1DS-br, HIV-1RC-br, and HIV-1YU-2, since the **anti-CCR5** antibody **2D7** was able to dramatically inhibit microglial infection by both wild-type and single-round luciferase pseudotype reporter viruses. Anti-CCR3 (7B11) and anti-CXCR4 (12G5) antibodies had little or no effect on infection. Last, the authors found that virus pseudotyped with the DS-br and RC-br envelopes can infect cells transfected with CD4 in conjunction with the G-protein-coupled receptors APJ, CCR8, and GPR15, which have been previously implicated in HIV entry.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:723554 CAPLUS
DOCUMENT NUMBER: 130:94276
TITLE: CCR5 has an expanded ligand-binding repertoire and is the primary receptor used by MCP-2 on activated T cells
AUTHOR(S): Ruffing, Nancy; Sullivan, Nancy; Sharmeen, Lamia; Sodroski, Joseph; Wu, Lijun
CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA
SOURCE: Cellular Immunology (1998), 189(2), 160-168
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CCR5 is a chemokine receptor expressed by T cells and macrophages, which also functions as the principal coreceptor for macrophage (M)-tropic HIV-1 strains to enter the host cells. Here, the authors aim to better understand the ligand-binding profiles of CCR5 and the chemokine-receptor usage on leukocytes. The authors found that MCP-2 could bind to CCR5 transfectants with high affinity and cross-compete effectively with RANTES, MIP-1 α , and MIP-1 β . MCP-2 is a true agonist for CCR5, eliciting a robust chemotactic response in CCR5 transfectants similar to that of the 3 known CCR5 ligands and exhibiting cross-desensitization with RANTES in the Ca²⁺ flux response. MCP-4 also bound to CCR5 with high affinity and was efficiently displaced by other CCR5 ligands. However, MCP-4 only partially displaced the binding of radiolabeled MIP-1 α and caused a chemotactic response only at high concns. Furthermore, MCP-2 inhibited the binding of the M-tropic HIV-1 gp120 envelope glycoprotein to CCR5 and HIV-1 infection of peripheral blood mononuclear cells. More importantly, the authors found that MCP-2 could bind and elicit chemotaxis in CD3-activated and IL-2-maintained T cells, and most of these functions could be specifically inhibited by the **anti-CCR5** mAb **2D7**, whereas the responses mediated by MIP-1 α or MCP-4 were only partially inhibited by **2D7**. Thus, although MCP-2 can bind to and signal through CCR1, CCR2b, and CCR5, among which both CCR2 and CCR5 are expressed at high levels on activated T cells, it appears to preferably utilize CCR5 on these cells. In contrast, MIP-1 α and MCP-4 seem to activate multiple receptors on the same cells. (c) 1998 Academic Press.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> "second extracellular loop"

498679 "SECOND"
11548 "SECONDS"
509535 "SECOND"
("SECOND" OR "SECONDS")
165053 "EXTRACELLULAR"
116571 "LOOP"
42940 "LOOPS"
144964 "LOOP"
("LOOP" OR "LOOPS")

L3 400 "SECOND EXTRACELLULAR LOOP"
("SECOND" (W) "EXTRACELLULAR" (W) "LOOP")

=> L3 and L1

L4 9 L3 AND L1

=> antibody and L4

285626 ANTIBODY

333616 ANTIBODIES

448218 ANTIBODY

(ANTIBODY OR ANTIBODIES)

L5 9 ANTIBODY AND L4

=> D L5 IBIB ABS 1-9

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:575989 CAPLUS

DOCUMENT NUMBER: 143:304430

TITLE: Novel vaccine strategy against AIDS using cyclic dodecapeptide mimicking the loop structure of HIV-1 coreceptor, CCR5

AUTHOR(S): Misumi, Shogo; Takamune, Nobutoki; Shoji, Shozo

CORPORATE SOURCE: Department of Pharmaceutical Biochemistry, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University, Kumamoto, 862-0973, Japan

SOURCE: Peptide Science (2005), Volume Date 2004, 41st, 343-346

CODEN: PSCIFQ; ISSN: 1344-7661

PUBLISHER: Japanese Peptide Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Monoclonal **antibody** KB8C12, raised against a cyclic closed-chain dodecapeptide (cDDR5) mimicking the **second extracellular loop** (Arg168-Cys178) of CCR5, recognized naive CCR5 mols., and inhibited CCR5-mediated HIV-1 infection. Furthermore, antisera from cynomolgus monkeys immunized with the cDDR5 displayed anti-HIV-1 activities. These results suggest that cDDR5 is a useful immunogen to induce a conformation-dependent **anti-CCR5 antibodies** capable of blocking HIV-1 infection.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:456295 CAPLUS

DOCUMENT NUMBER: 143:24660

TITLE: Identification of a linear peptide recognized by monoclonal **antibody** 2D7 capable of generating CCR5-specific **antibodies** with human immunodeficiency virus-neutralizing activity

AUTHOR(S): Khurana, Surender; Kennedy, Michael; King, Lisa R.; Golding, Hana

CORPORATE SOURCE: Division of Viral Products, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, Bethesda, MD, 20892, USA

SOURCE: Journal of Virology (2005), 79(11), 6791-6800

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CCR5 is the major coreceptor for human immunodeficiency virus (HIV) infection. The murine monoclonal **antibody** (MAb) 2D7, which recognizes a conformation-dependent epitope in the **second extracellular loop** of CCR5, is one of the most potent inhibitors of R5 virus cell entry. However, attempts to humanize 2D7 for in vivo human use have been unsuccessful so far. A filamentous phage library expressing random peptides was used to identify a peptide mimotope that is recognized by MAb 2D7. A synthetic peptide containing this sequence (2D7-2SK) bound to MAb 2D7 with high affinity and reversed its HIV type 1 (HIV-1) fusion inhibitory activity. The peptide contains sequence homologies to two distal regions of the **second extracellular loop** of human CCR5, both of which are required for MAb 2D7 binding. Rabbit anti-2D7-mimotope **antibodies** competed with MAb 2D7 for binding to the 2D7-2SK peptide in Biacore

biosensor testing. Importantly, the rabbit anti-2D7-2SK **antibodies** bound to CCR5 on cells and specifically inhibited R5 (but not X4) envelope-mediated syncytium formation. These **antibodies** also neutralized infection of human peripheral blood mononuclear cells with R5 HIV isolates comparably to MAb 2D7. In summary, the authors have identified a novel peptide that closely mimics the MAb 2D7 epitope on CCR5. This peptide could be included as a potential vaccine candidate or to isolate 2D7-like human **antibodies** as entry inhibitors for R5 viruses.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:427593 CAPLUS

DOCUMENT NUMBER: 143:24658

TITLE: Natural **Antibodies** to CCR5 from Breast Milk Block Infection of Macrophages and Dendritic Cells with Primary R5-Tropic HIV-1

AUTHOR(S): Bouhlal, Hicham; Latry, Vanessa; Requena, Mary; Aubry, Sylvie; Kaveri, Srinivas V.; Kazatchkine, Michel D.; Belec, Laurent; Hocini, Hakim

CORPORATE SOURCE: Institut Nationale de la Sante et de la Recherche Medicale (INSERM) U743, Equipe d'Immunité et Biotherapies Muqueuses et Université René Descartes Paris V, Institut Biomedical des Cordeliers, Paris, 75006, Fr.

SOURCE: Journal of Immunology (2005), 174(11), 7202-7209 CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present study, the authors demonstrate that breast milk of 66% and 83% of HIV-seroneg. and seropos. women, resp., contains natural Abs of the secretory IgA and IgG isotypes directed against the CCR5 coreceptor for R5-tropic strains of HIV-1. Abs to CCR5 were affinity purified on a matrix to which a synthetic peptide corresponding to the **second extracellular loop** of CCR5 had been coupled. The purified Abs bound to the CCR5 peptide in a dose-dependent fashion and to both native CCR5 expressed by Chinese hamster ovary cells transfected with CCR5 gene, macrophages, and immature dendritic cells. Although the avidity differed, the amount of **anti-CCR5** Abs did not significantly differ between breast milk of HIV-seropos. and -seroneg. women. Purified **anti-CCR5** Abs inhibited up to 75% infection of macrophages and dendritic cells with HIVBaL and HIVJR-CSF. These observations provide evidence for a role of natural Abs to CCR5 in breast milk in controlling transmissibility of HIV through breast feeding.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1046453 CAPLUS

DOCUMENT NUMBER: 142:175004

TITLE: Soluble chemokine CCR5 receptor is present in human plasma

AUTHOR(S): Tsimanis, Alexander; Kalinkovich, Alexander; Bentwich, Zvi

CORPORATE SOURCE: R. Ben-Ari Institute of Clinical Immunology and AIDS Center, Kaplan Medical Center, Hebrew University Hadassah Medical School, Rehovot, Israel

SOURCE: Immunology Letters (2005), 96(1), 55-61 CODEN: IMLED6; ISSN: 0165-2478

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In view of the natural resistance to infection by HIV and occasional delayed clin. manifestation of the disease, as also the fact that the virus is able to enter only cells that express CD4 and a co-receptor, we initiated a search for a soluble co-receptor that might compete with its membrane counterpart. Using a sandwich ELISA system, a soluble human CCR5

receptor (sCCR5) was indeed detected in the circulation. Immunopptn. of sCCR5-pos. plasma samples from Israelis of Ethiopian and non-Ethiopian origin with mAb 2D7, a conformation-dependent **anti-CCR5 antibody**, revealed the presence of a .apprx.22 kDa protein. A panel of **antibodies** directed against the membrane receptor was used to characterize the structure of the soluble CCR5: mAb CTC8, recognizing the N-terminal sequence of the protein, 10YDIN13; "multidomain" mAbs FAB181B and FAB183B that are dependent upon the presence of Q93 and D95 in ECL1 and K171 and E172 in ECL2A, and mAb FAB182B, recognizing the stretch 184YSQYQF189, which spans the C-terminal part of the **second extracellular loop**. The presence of short soluble CCR5 in human plasma has not been previously described. Among HIV-neg. non-Ethiopian Israelis, 20.4% were sCCR5-pos., as against only 10.5% in HIV-positives. However, 7.1% of HIV-neg. Ethiopian Israelis were sCCR5 pos., as were 5.6% HIV-positives. Plasma concns. of MIP-1 β , the CCR5 agonist, were twice as high in sCCR5-positives (140.8 ± 25.8 pg/mL) as in the sCCR5-negatives (77.6 ± 11.0 pg/mL, $P = 0.0157$). A significant pos. correlation between plasma levels of sCCR5 and MIP-1 β was found (Fig. 4, $r = 0.8$, $P < 0.0001$).

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:318783 CAPLUS

DOCUMENT NUMBER: 139:173234

TITLE: Analysis of the mechanism by which the small-molecule CCR5 antagonists SCH-351125 and SCH-350581 inhibit human immunodeficiency virus type 1 entry

AUTHOR(S): Tsamis, Fotini; Gavrillov, Svetlana; Kajumo, Francis; Seibert, Christoph; Kuhmann, Shawn; Ketas, Tom; Trkola, Alexandra; Palani, Anadan; Clader, John W.; Tagat, Jayaram R.; McCombie, Stuart; Baroudy, Bahige; Moore, John P.; Sakmar, Thomas P.; Dragic, Tatjana

CORPORATE SOURCE: Microbiology and Immunology Department, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Journal of Virology (2003), 77(9), 5201-5208

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human immunodeficiency virus type 1 (HIV-1) entry is mediated by the consecutive interaction of the envelope glycoprotein gp120 with CD4 and a coreceptor such as CCR5 or CXCR4. The CCR5 coreceptor is used by the most commonly transmitted HIV-1 strains that often persist throughout the course of infection. Compds. targeting CCR5-mediated entry are a novel class of drugs being developed to treat HIV-1 infection. In this study, we have identified the mechanism of action of two inhibitors of CCR5 function, SCH-350581 (AD101) and SCH-351125 (SCH-C). AD101 is more potent than SCH-C at inhibiting HIV-1 replication in primary lymphocytes, as well as viral entry and gp120 binding to cell lines. Both mols. also block the binding of several **anti-CCR5 monoclonal antibodies** that recognize epitopes in the **second extracellular loop** of CCR5. Alanine mutagenesis of the transmembrane domain of CCR5 suggests that AD101 and SCH-C bind to overlapping but nonidentical sites within a putative ligand-binding cavity formed by transmembrane helices 1, 2, 3, and 7. We propose that the binding of small mols. to the transmembrane domain of CCR5 may disrupt the conformation of its extracellular domain, thereby inhibiting ligand binding to CCR5.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:283870 CAPLUS

DOCUMENT NUMBER: 136:368158

TITLE: Multiple active states and oligomerization of CCR5 revealed by functional properties of monoclonal **antibodies**

AUTHOR(S): Blanpain, Cedric; Vanderwinden, Jean-Marie; Cihak,

Josef; Wittamer, Valerie; Le Poul, Emmanuel; Issafras, Hassan; Stangassinger, Manfred; Vassart, Gilbert; Marullo, Stefano; Schlondorff, Detlef; Parmentier, Marc; Mack, Matthias

CORPORATE SOURCE:

Institut de Recherche Interdisciplinaire en Biologie Humaine et Nucleaire, Universite Libre de Bruxelles, Brussels, B-1070, Belg.

SOURCE:

Molecular Biology of the Cell (2002), 13(2), 723-737
CODEN: MBCEEV; ISSN: 1059-1524

PUBLISHER:

American Society for Cell Biology

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB CC-chemokine receptor 5 (CCR5) is the principal coreceptor for macrophage-tropic strains of human immunodeficiency virus type 1 (HIV-1). The authors have generated a set of **anti-CCR5** monoclonal **antibodies** and characterized them in terms of epitope recognition, competition with chemokine binding, receptor activation and trafficking, and coreceptor activity. MC-4, MC-5, and MC-7 mapped to the amino-terminal domain, MC-1 to the **second extracellular loop**, and MC-6 to a conformational epitope covering multiple extracellular domains. MC-1 and MC-6 inhibited regulated on activation normal T cell expressed and secreted (RANTES), macrophage inflammatory polypeptide-1 β , and Env binding, whereas MC-5 inhibited macrophage inflammatory polypeptide-1 β and Env but not RANTES binding. MC-6 induced signaling in different functional assays, suggesting that this monoclonal **antibody** stabilizes an active conformation of CCR5. Flow cytometry and real-time confocal microscopy showed that MC-1 promoted strong CCR5 endocytosis. MC-1 but not its monovalent isoforms induced an increase in the transfer of energy between CCR5 mols. Also, its monovalent isoforms bound efficiently, but did not internalize the receptor. In contrast, MC-4 did not prevent RANTES binding or subsequent signaling, but inhibited its ability to promote CCR5 internalization. These results suggest the existence of multiple active conformations of CCR5 and indicate that CCR5 oligomers are involved in an internalization process that is distinct from that induced by the receptor's agonists.

REFERENCE COUNT:

64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:645176 CAPLUS

DOCUMENT NUMBER:

135:343097

TITLE:

Adaptation to Blockade of Human Immunodeficiency Virus Type 1 Entry Imposed by the **Anti-CCR5** Monoclonal **Antibody** 2D7

AUTHOR(S):

Aarons, Emma J.; Beddows, Simon; Willingham, Tim; Wu, Lijun; Koup, Richard A.

CORPORATE SOURCE:

Department of Medicine, Division of Infectious Disease, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA

SOURCE:

Virology (2001), 287(2), 382-390
CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER:

Academic Press

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The **second extracellular loop** (ECL2) domain of CC-chemokine receptor 5 (CCR5) has been proposed as a specific target site for therapeutic agents aimed at blocking CCR5-dependent entry by human immunodeficiency virus type I (HIV-1). We have adapted two CCR5-using HIV-1 isolates, prototypic JR-CSF, and a primary isolate, 11-121, to replicate in vitro in the presence of high concns. of a monoclonal **antibody** (MAb 2D7) specific for the CCR5 ECL2 domain. The 75% inhibitory concns. (IC75) for the two 2D7-adapted isolates were approx. 100-fold higher than those for corresponding control isolates passaged without the MAb. Adapted isolates did not acquire the ability to use CXCR4, CCR3, or CCR1. Env clones derived from MAb 2D7-adapted JR-CSF showed several gp120 mutations that were not found in any of the control JR-CSF clones. The in vitro observations suggest that CCR5-using HIV-1 strains might also be able to adapt in vivo to evade an ECL2-blocking therapeutic agent. (c) 2001 Academic Press.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:399156 CAPLUS

DOCUMENT NUMBER: 135:179630

TITLE: Human α 1-acid glycoprotein binds to CCR5
expressed on the plasma membrane of human primary
macrophages

AUTHOR(S): Atemezem, Aurelie; Mbemba, Elisabeth; Vassy, Roger;
Slimani, Hocine; Saffar, Line; Gattegno, Liliane

CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, JE 2138, Faculte
de Medecine Leonard de Vinci, Universite Paris XIII,
Bobigny, 93017, Fr.

SOURCE: Biochemical Journal (2001), 356(1), 121-128

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have reported previously that human α 1-acid glycoprotein (AGP) inhibits the infection of human monocyte-derived macrophages (MDM) by R5 HIV-1, and that a disulfide-bridged peptide mimicking the clade B HIV-1 gp120 consensus V3 domain (V3Cs) binds specifically to CCR5 (the major co-receptor of R5 HIV strains) on these cells. The present study demonstrates that AGP binds specifically to MDM at high- and low-affinity binding sites with K_d values of 16 nM and 4.9 μ M resp. The fact that heat denaturation of AGP only partly inhibited this binding (43%) suggests that protein-protein interactions are involved, as well as AGP glycans which are resistant to heat denaturation. Mannan, but not dextran, is a significant inhibitor (52%) of this binding, and sequential exoglycosidase treatment of AGP, which exposes penultimate mannose residues, has a strong stimulatory effect (.apprx. 2.8-fold). Therefore AGP glycans (probably mannose residues) are involved, at least partly, in the binding of AGP to MDM. In addition, AGP inhibits the binding of V3Cs and macrophage inflammatory protein-1 β (MIP-1 β) to MDM. The **anti-CCR5** monoclonal **antibody** 2D7, specific for the **second extracellular loop** of CCR5, also inhibited AGP binding (67%), whereas **anti-CCR5 antibodies** specific for the C-terminus of CCR5 region had no effect. Native AGP, like V3Cs (but not heat-denatured AGP), binds to 46 and 33-36 kDa electroblotted AGP-bound MDM membrane ligands, characterized as CCR5 by their interactions with **anti-CCR5 antibodies** and with MIP-1 β . Therefore both AGP glycans and MDM CCR5 are involved in the binding of AGP to MDM. This suggests that the inhibitory effect of AGP on the infection of human primary macrophages by R5 HIV-1 may be related to specific binding of AGP to a macrophage membrane lectin or lectin-like component and to CCR5.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:263464 CAPLUS

DOCUMENT NUMBER: 131:57557

TITLE: Differential inhibition of human immunodeficiency
virus type 1 fusion, gp120 binding, and CC-chemokine
activity by monoclonal **antibodies** to CCR5

AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima,
Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.;
Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah
A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.;
Maddon, Paul J.; Dragic, Tatjana

CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller
University, New York, NY, 10016, USA

SOURCE: Journal of Virology (1999), 73(5), 4145-4155

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most

commonly transmitted human immunodeficiency virus type 1 (HIV-1) strains. The authors have isolated 6 new **anti-CCR5** murine monoclonal **antibodies** (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb 2D7 to specific amino acid residues in the N terminus and/or **second extracellular loop** regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) HIV-1 entry, (2) HIV-1 envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit HIV-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited HIV-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and 2D7, the most potent inhibitors of HIV-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting HIV-1 entry and fusion, PA12 but not PA14 was potentially synergistic when used in combination with 2D7, RANTES, and CD4-IgG2, which inhibits HIV-1 attachment. The data support a model wherein HIV-1 entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These **antibodies** will be useful for further dissecting these events.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> "GC-CKR5"
200943 "CC"
1047 "CCS"
201866 "CC"
("CC" OR "CCS")
28 "CKR5"
L6 18 "CC-CKR5"
("CC"(W) "CKR5")

=> antibody and L6
285626 ANTIBODY
333616 ANTIBODIES
448218 ANTIBODY
(ANTIBODY OR ANTIBODIES)
L7 5 ANTIBODY AND L6

=> D L7 IBIB ABS 1-5

L7 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:499783 CAPLUS
DOCUMENT NUMBER: 135:103329
TITLE: Methods of identifying G protein-coupled receptors
associated with the uptake of macrophage-trophic HIV,
and their use in diagnosis and treatment of AIDS
INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried;
Landau, Nathaniel R.; Liu, Rong
PATENT ASSIGNEE(S): The Aaron Diamond Aids Research Center, USA; New York
University
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 858,660,
abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6258527	B1	20010710	US 1997-861105	19970521
US 2003096221	A1	20030522	US 2000-734221	20001211
PRIORITY APPLN. INFO.:			US 1996-17157P	P 19960520
			US 1996-20043P	P 19960619
			US 1997-858660	B2 19970519
			US 1997-861105	A1 19970521

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as
addnl. host cell cofactors. A cofactor required for infection with virus
adapted for growth in transformed T cell lines was recently identified and
named fusin. Fusin, however, does not promote entry of macrophage-tropic
viruses that are believed to be the key pathogenic strains in vivo. It
has now been determined that the principal cofactor for entry mediated by the
envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is
CC-CKR5, a receptor for the β -chemokines RANTES,
MIP-1 α , and MIP-1 β . The uptake of the virus may be blocked by
ligands for the receptor or by preventing the receptor gene expression and
in control of the synergism between infection by other viruses and the
spread of HIV into other cell types. Expts. with viruses pseudotyped with
different env glycoproteins showed that uptake was dependent upon the
presence of chemokine receptors with different serotypes of the virus
showing different receptor requirements. Methods of using chemokine
receptor-deficient host cells as expression hosts to identify receptor
requirements of clin. isolates of HIV-1 are described.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:229024 CAPLUS
DOCUMENT NUMBER: 128:279581
TITLE: Cloning, sequence, and expression of a mouse genomic

clone for the **CC-CKR5** receptor and construction of knockout mutations
 INVENTOR(S): Bergsma, Derk J.; Brawner, Mary E.; Shabon, Usman
 PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
 SOURCE: Eur. Pat. Appl., 27 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 834564	A2	19980408	EP 1997-307823	19971003
EP 834564	A3	19980513		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6388055	B1	20020514	US 1996-724984	19961003
JP 10179180	A2	19980707	JP 1997-307784	19971003
PRIORITY APPLN. INFO.:			US 1996-724984	A 19961003

AB Mouse chemokine receptor **CC-CKR5** polypeptides and DNA (RNA) encoding such mouse **CC-CKR5** and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such mouse **CC-CKR5** in the development of gene knockout mice for use as a model for human immunodeficiency virus.. Expression vectors carrying the **CC-CKR5** gene are constructed and expressed in human embryonic kidney 293 cells. **Antibodies** to **CC-CKR5** are also claimed.

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:772659 CAPLUS
 DOCUMENT NUMBER: 128:33766
 TITLE: Methods of identifying G-coupled receptors associated with macrophage-trophic HIV, and diagnostic and therapeutic uses thereof
 INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried; Landau, Nathaniel R.; Liu, Rong
 PATENT ASSIGNEE(S): New York University, USA
 SOURCE: PCT Int. Appl., 83 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744055	A1	19971127	WO 1997-US8926	19970520
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5939320	A	19990817	US 1996-666020	19960619
AU 9731434	A1	19971209	AU 1997-31434	19970520
PRIORITY APPLN. INFO.:			US 1996-17157P	P 19960520
			US 1996-650412	A 19960520
			US 1996-666020	A 19960619
			WO 1997-US8926	W 19970520

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as addnl. host cell cofactors. A cofactor required for infection with virus adapted for growth in transformed T cell lines was recently identified and named fusin. Fusin, however, does not promote entry of macrophage-tropic viruses that are believed to be the key pathogenic strains in vivo. It has now been determined that the principal cofactor for entry mediated by the envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is

CC-CKR5, a receptor for the β -chemokines RANTES, MIP-1 α , and MIP-1 β . The cofactor is useful for screening of drugs capable of modulating the production of a translocation promoting agent and capable of treating AIDS.

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:459509 CAPLUS
DOCUMENT NUMBER: 127:173725
TITLE: Development of resistance of human immunodeficiency virus type 1 to dextran sulfate associated with the emergence of specific mutations in the envelope gp 120 glycoprotein
AUTHOR(S): Este, Jose A.; Schols, Dominique; De Vreese, Karen; Van Laethem, Kristel; Vandamme, Anne-Mieke; Desmyter, Jan; De Clercq, Erik
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SOURCE: Molecular Pharmacology (1997), 52(1), 98-104
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyanionic compds. are known to inhibit the binding of human immunodeficiency virus (HIV) to CD4+ cells and the subsequent fusion step between the virus and cells. An HIV-1 strain resistant to dextran sulfate (DS) was selected by cultivation of HIV-1 (NL4-3)-infected MT-4 cells in the presence of DS Mr 5000. DS did not inhibit the binding of DS-resistant virus to MT-4 cells or syncytium formation between MOLT cells and HUT-78 cells persistently infected with the DS-resistant virus. In addition, a monoclonal **antibody** with specificity for the V3 loop of envelope gp120 glycoprotein did not recognize the DS-resistant HIV-1 gp120 V3 loop. The following mutations were found in the gp120 mol. of the DS-resistant HIV-1 strain but not in the wild-type strain: S114N in the V1 loop region; S134N in the V2 loop region; K269E, Q278H, and N293D in the V3 loop region; N323S in the C3 region; a deletion of 5 amino acids (Phe-Asn-Ser-Thr-Trp) at positions 364-368 in the V4 loop; and R387I in the CD4 binding domain. These results suggest that (i) DS interacts with specific amino acid residues in the gp 120 mol., (ii) the virus is able to overcome the inhibitory effect of DS on viral infectivity, (iii) cross-resistance developed against those polyanionic compds. that are structurally related to DS, and (iv) the mol. determinants of HIV cell tropism, syncytium-inducing ability, coreceptor (fusin/CC-CKR5) utilization, and polyanion resistance seem to be located in the env genome of HIV and specifically in the V3 loop domain.

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:433148 CAPLUS
DOCUMENT NUMBER: 125:112550
TITLE: Cell type-specific fusion cofactors determine human immunodeficiency virus type 1 tropism for T-cell lines versus primary macrophages
AUTHOR(S): Alkhatib, Ghalib; Broder, Christopher C.; Berger, Edward A.
CORPORATE SOURCE: Lab. Viral Dis., Natl. Inst. Allergy and Infectious Dis., Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (1996), 70(8), 5487-5494
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Work in this laboratory previously demonstrated that the tropism of different human immunodeficiency type 1 isolates for infection of human CD4+ continuous cell lines (e.g., T-cell lines and HeLa-CD4 transformants) vs. primary macrophages is associated with parallel intrinsic fusogenic specificities of the corresponding envelope glycoproteins (Envs). For T-cell line-tropic isolates, it is well established that the target cell must also contain a human-specific fusion cofactor(s) whose identity is unknown. In this study, we tested the hypothesis that the Env fusion specificities underlying T-cell line vs. macrophage tropism are determined by

distinct cell type-specific fusion cofactors. We applied a recombinant vaccinia virus-based reporter gene assay for Env-CD4-mediated cell fusion; the LAV and Ba-L Envs served as prototypes for T-cell line-tropic and macrophage-tropic isolates, resp. We examined CD4+ promyelocytic and monocytic cell lines that are infectible by T-cell line-tropic isolates and become susceptible to macrophage-tropic strains only after treatment with differentiating agents. We observed parallel changes in fusion specificity: untreated cells supported fusion by the LAV but not the Ba-L Env, whereas cells treated with differentiating agents acquired fusion competence for Ba-L. These results suggest that in untreated cells, the block to infection by macrophage-tropic isolates is at the level of membrane fusion; furthermore, the differential regulation of fusion permissiveness for the two classes of Envs is consistent with the existence of distinct fusion cofactors. To test this notion directly, we conducted expts. with transient cell hybrids formed between CD4-expressing nonhuman cells (murine NIH 3T3) and different human cell types. Hybrids formed with HeLa cells supported fusion by the LAV Env but not by the Ba-L Env, whereas hybrids formed with primary macrophages showed the opposite specificity; hybrids formed between HeLa cells and macrophages supported fusion by both Envs. These results suggest the existence of cell type-specific fusion cofactors selective for each type of Env, rather than fusion inhibitors for discordant Env-cell combinations. Finally, analyses based on recombinant protein expression and **antibody** blocking did not support the proposals by others that the CD44 or CD26 antigens are involved directly in the entry of macrophage-tropic isolates.